

### REMARKS

Claims 1-25 are pending in this application. Claims 18-21 have been withdrawn from consideration as being drawn to a non-elected invention. Claims 1 and 25 have been amended.

Claims 1 and 25 have been amended for the sole reason of advancing prosecution. Applicants, by amending any claims herein, make no admission as to the validity of any rejection made by the Examiner against any of these claims. Applicants reserve the right to reassert any of the claims canceled herein or the original claim scope of any claim amended herein, in a continuing application.

Each of claims 1 and 25 have been amended to recite "...g) outputting the expanded all-atom representation of the amino acid sequence obtained in step (f), wherein at least steps (b) – (f) are preformed on a sufficiently programmed computer." Support for claims 1 and 25, as amended, can be found throughout the specification and claims as originally filed.

No new matter has been added.

In view of the foregoing, further and favorable consideration is respectfully requested.

***I. Interview***

Applicants thank Examiner Lin and Supervisor Examiner Moran for conducting a telephone interview with Applicants' undersigned representative on April 1, 2009. Applicants specifically thank the Examiners for the indication that the claims, as amended herein, would appear to overcome the rejections under both 35 USC §§ 101 and 103.

***II. At page 2 of the Official Action, claims 1-17 and 22-28 have been rejected under 35 USC § 101.***

The Examiner asserts that claims 1-17 and 22-28 are directed to non-statutory subject matter because the claims are not tied to a machine and do not allegedly require a tangible final result.

In view of the following, this rejection is respectfully traversed.

The U.S. Court of Appeals for the Federal Circuit very recently held in *In re Bilski*, 545 F.3d 943 (2008), that "a claimed process is surely patent-eligible under § 101 if: (1) it is tied to a particular machine or apparatus, *or* (2) it transforms a particular article into a different state or thing. ...the mere fact that a claimed invention involves inputting numbers, calculating numbers, outputting numbers, and storing numbers, in and of itself, would not render it nonstatutory subject matter. The same reasoning applies when the claim at issue recites fundamental principles other than mathematical algorithms. Thus the proper inquiry under § 101 is not whether the process claim recites sufficient 'physical steps,' but rather whether the claim meets the machine-or-transformation test. As a result, even a claim that recites 'physical steps' but neither recites a particular machine or apparatus, nor transforms any article into a different state or thing, is not drawn to patent-eligible subject matter.

Conversely, a claim that purportedly lacks any “physical steps” but is still tied to a machine or achieves an eligible transformation passes muster under § 101.” *In re Bilski*, 545 F.3d at 961.

The Federal Circuit further held that meeting the “useful, concrete and tangible result” test from *State Street* is inadequate to establish patentability. The Court explained: “to be sure, a process tied to a particular machine, or transforming or reducing a particular article into a different state or thing, will generally produce a ‘concrete’ and ‘tangible’ result as those terms were used in our prior decisions. But while looking for a ‘useful, concrete and tangible result’ may in many circumstances provide useful indications of whether a claim is drawn to a fundamental principle or a practical application of such a principle, that inquiry is insufficient to determine whether a claim is patent-eligible under 101. And it was never meant to supplant the Supreme Court’s test. Therefore, we also conclude that the ‘useful, concrete and tangible result’ inquiry is inadequate and reaffirm that the machine-or-transformation test outlined by the Supreme Court is the proper test to apply.” *Id.* at 959. *See also, State Street Bank & Trust Co. v. Signature Financial Group, Inc.*, 149 F.3d 1368 (Fed. Cir. 1998).

Applicants respectfully submit that pending claims 1-17 and 22-28 are directed to statutory subject matter under 35 USC § 101 because the presently claimed subject matter meets all of the requirements for statutory subject matter in view of the recent *In re Bilski* decision. In this regard, Applicants note that claim 1 has been amended to recite that “...g) outputting the expanded all-atom representation of the amino acid sequence obtained in step (f), wherein at least steps (b) – (f) are preformed on a sufficiently programmed

computer.” Accordingly, the present subject matter meets the aforementioned machine test set forth by *In re Bilski*.

In view of the remarks set forth herein, it is submitted that claims 1-15 and 22-25 are directed to patentable subject matter within the meaning of 35 USC §101. Thus, the Examiner is respectfully requested to withdraw this rejection.

**IV. At page 4 of the Official Action, claims 1-5, 9-17, 22 and 23 have been rejected under 35 USC § 103 as being unpatentable over Dahiyat et al. in view of Herzyk et al.**

The Examiner asserts that it would have been obvious to the skilled artisan “to combine the teaching of Dahiyat et al.” The Examiner reasons that “one of ordinary skill in the art could have taken the data of Dahiyat et al. and represented that data in the teachings of Herzyk et al.” and that “one of ordinary skill in the art could have combined the elements as claimed by known methods with no change in their respective functions.”

In view of the following these rejections are respectfully traversed.

To establish a *prima facie* case of obviousness, the Examiner must satisfy three requirements. First, as the U.S. Supreme Court very recently held in *KSR International Co. v. Teleflex Inc.*, 550 U.S. 398 (2007), “a court must ask whether the improvement is more than the predictable use of prior art elements according to their established functions. ...it [may] be necessary for a court to look to interrelated teachings of multiple patents; the effects of demands known to the design community or present in the marketplace; and the background knowledge possessed by a person having ordinary skill in the art, all in order to determine whether there was an apparent reason to combine the known elements in the

fashion claimed by the patent at issue. ...it can be important to identify a reason that would have prompted a person of ordinary skill in the relevant field to combine the elements in the way the claimed new invention does... because inventions in most, if not all, instances rely upon building blocks long since uncovered, and claimed discoveries almost of necessity will be combinations of what, in some sense, is already known." (*KSR*, 550 U.S. 398 at 417.) Second, the proposed modification of the prior art must have had a reasonable expectation of success, determined from the vantage point of the skilled artisan at the time the invention was made. *Amgen Inc. v. Chugai Pharm. Co.*, 18 USPQ2d 1016, 1023 (Fed. Cir. 1991). Lastly, the prior art references must teach or suggest all the limitations of the claims. *In re Wilson*, 165 USPQ 494, 496 (C.C.P.A. 1970).

Independent claim 1 is directed to a computer-implemented method for predicting at least one amino acid sequence that folds into a specified three-dimensional (3D) structure of a predetermined reference protein or peptide, the at least one amino acid sequence having a biological activity the same as a biological activity of the reference protein or peptide; which method comprises the steps of: a) providing a coordinate set representing the backbone of the 3D structure; b) constructing a reduced virtual representation for the 3D structure provided in step (a), wherein in the reduced representation, each amino acid has a backbone portion and a side chain portion, the backbone portion of each amino acid being represented by a single sphere and the side chain of each amino acid being represented by one to three additional spheres; c) determining for each amino acid position along the virtual structure representation provided in step (b) its solvent accessibility; d) constructing an initial amino acid sequence by assigning for each amino acid position along

the structure an amino acid residue selected randomly from a predefined group of amino acids having a solvent accessibility compatible with the solvent accessibility of the position;

e) randomly selecting one or more positions along the sequence provided in step (d) and applying on each position a Monte-Carlo simulation in sequence space and rotamer space, the simulation comprising one or more scoring function calculating steps which include: i) randomly selecting one or more amino acid residues of the same solvent accessibility as that defined for the position to obtain a mutation; ii) for each of the one or more selected positions, calculating an energy difference  $\Delta E$ , between the amino acid residue at the position in the predetermined protein or peptide and each of the one or more selected amino acid residues provided in step (i) based on its the reduced virtual representation; iii) selecting a rotamer having a minimal  $\Delta E$ , or when more than one amino acid are manipulated simultaneously, selecting a rotamer combination having a minimal  $\Delta E$ ; iv) accepting the mutation with the rotamer or rotamer combination selected in step (iii) if  $\Delta E < 0$ ; and v) assigning the amino acid residue or residues and their respective selected rotamer or rotamer combinations selected in step (iii) to the position(s) and moving to another position along the sequence; wherein the simulation steps are repeated until for each position along the sequence, the residue and residue's rotamer with the lowest energy score is selected, to obtain a virtually represented amino acid sequence with the lowest total energy score; f) expanding the reduced representation of the virtually represented amino acid sequence obtained in step (e) to its corresponding all-atom sequence representation thereby obtaining an amino acid sequence compatible with the structure of the predetermined protein or peptide; and g) outputting the expanded all-atom

representation of the amino acid sequence obtained in step (f), wherein at least steps (b)–(f) are preformed on a sufficiently programmed computer. Claims 2-5, 9-17, 22 and 23 depend, either directly or indirectly, from claim 1.

In contrast to the presently pending subject matter neither Dahiyat et al. nor Herzyk et al. teach or suggest the subject matter recited in the presently pending claims. More specifically, Applicants submit that, whether taken alone or in combination, neither Dahiyat et al. nor Herzyk et al. teach or suggest “g) outputting the expanded all-atom representation of the amino acid sequence obtained in step (f)...,” as recited in claim 1.

In view of the foregoing, it is submitted that nothing in any of Dahiyat et al. and Herzyk et al., taken alone or together, renders the claimed subject matter obvious within the meaning of 35 USC §103. Accordingly, the Examiner is respectfully requested to withdraw this rejection.

***V. At page 8 of the Official Action, claims 6-8 have been rejected under 35 USC § 103 as being unpatentable over Dahiyat et al. in view of Herzyk et al., and in further view of Hurley et al.***

The Examiner asserts that neither Dahiyat et al. nor Herzyk et al. teaches that the solvent is substantially water, but that it would have been obvious to the skilled artisan “to combine the teaching of Dahiyat et al., Herzyk et al. and those of Hurley et al.” as Hurley et al. teach that “it would have been obvious to determine the structure of an amino acid in water because it would have allowed for the calculation of stability.”

In view of the following these rejections are respectfully traversed.

To establish a *prima facie* case of obviousness, the Examiner must satisfy three requirements. First, as the U.S. Supreme Court very recently held in *KSR International Co. v. Teleflex Inc.*, 550 U.S. 398 (2007), "a court must ask whether the improvement is more than the predictable use of prior art elements according to their established functions. ...it [may] be necessary for a court to look to interrelated teachings of multiple patents; the effects of demands known to the design community or present in the marketplace; and the background knowledge possessed by a person having ordinary skill in the art, all in order to determine whether there was an apparent reason to combine the known elements in the fashion claimed by the patent at issue. ...it can be important to identify a reason that would have prompted a person of ordinary skill in the relevant field to combine the elements in the way the claimed new invention does... because inventions in most, if not all, instances rely upon building blocks long since uncovered, and claimed discoveries almost of necessity will be combinations of what, in some sense, is already known." (*KSR*, 550 U.S. 398 at 417.) Second, the proposed modification of the prior art must have had a reasonable expectation of success, determined from the vantage point of the skilled artisan at the time the invention was made. *Amgen Inc. v. Chugai Pharm. Co.*, 18 USPQ2d 1016, 1023 (Fed. Cir. 1991). Lastly, the prior art references must teach or suggest all the limitations of the claims. *In re Wilson*, 165 USPQ 494, 496 (C.C.P.A. 1970).

Claim 1 is discussed above with regard to the previous rejection. The discussion of claim 1 is incorporated herein by reference. Claims 6-8 depend, either directly or indirectly, from claim 1.



As discussed, in contrast to the presently pending subject matter neither Dahiyat et al. nor Herzyk et al. teach or suggest the subject matter recited in the presently pending claims. More specifically, Applicants submit that, whether taken alone or in combination, neither Dahiyat et al. nor Herzyk et al. teach or suggest “g) outputting the expanded all-atom representation of the amino acid sequence obtained in step (f)...,” as recited in claim 1.

Hurley et al. do not remedy the deficiencies of Dahiyat et al. and Herzyk et al. Like Dahiyat et al. and Herzyk et al., Hurley et al. do not teach or suggest suggest “g) outputting the expanded all-atom representation of the amino acid sequence obtained in step (f)...,” as recited in claim 1. Accordingly, Applicants submit that none of the cited references teach or suggest every element of the presently claimed subject matter.

In view of the foregoing, it is submitted that nothing in any of Dahiyat et al., Herzyk et al. and Hurley et al., taken alone or together, renders the claimed subject matter obvious within the meaning of 35 USC §103. Accordingly, the Examiner is respectfully requested to withdraw this rejection.


### **Conclusion**

In view of the foregoing, Applicants submit that the application is in condition for immediate allowance. Early notice to that effect is earnestly solicited. The Examiner is invited to contact the undersigned attorney if it is believed that such contact will expedite the prosecution of the application.

In the event this paper is not timely filed, Applicants petition for an appropriate extension of time. Please charge any fee deficiency or credit any overpayment to Deposit Account No. 14-0112.

Respectfully submitted,

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Date: May 21, 2009  
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